



**University of
Zurich**^{UZH}

**Zurich Open Repository and
Archive**

University of Zurich
University Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2020

Stage-related PD-L1 expression in Kaposi sarcoma tumor microenvironment

Joest, Beatrice ; Kempf, Werner ; Berisha, Arbeneshe ; Peyk, Peter ; Tronnier, Michael ; Mitteldorf, Christina

Abstract: Background The immune checkpoint molecule PD-L1 represents an important target in oncological immune therapy. The aim of our study was to evaluate PD-L1 expression and the composition of the tumor microenvironment (TME) in Kaposi sarcoma. Methods Immunohistochemical stains were performed for PD-L1, CD3, CD33, CD68, and CD168 in 24 Kaposi sarcoma samples. In PD-L1-positive cases, the double stains for PD-L1, CD31, podoplanin, and HHV8 were added. Results PD-L1 was observed in 71% of the samples and was predominantly located in the TME. PD-L1 expression was significantly higher in nodular stage than in patch/plaque stage. The TME consisted of CD68+/CD163+ macrophages, CD33+ myeloid-derived suppressor cells and monocytes and CD3+ T-cells. The TME showed a peritumoral distribution in nodular stage, in contrast to a diffuse distribution in patch/plaque stage. In 12 samples (50%), no plasma cells were found. Conclusion In nodular stage of KS, the TME is pushed back in the periphery of the tumor nodules. The PD-L1-positive TME between the tumor cells might protect them from the immune attack. An anti-PD-L1 treatment might be promising in KS patients.

DOI: <https://doi.org/10.1111/cup.13716>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-199958>

Journal Article

Published Version



The following work is licensed under a Creative Commons: Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) License.

Originally published at:

Joest, Beatrice; Kempf, Werner; Berisha, Arbeneshe; Peyk, Peter; Tronnier, Michael; Mitteldorf, Christina (2020). Stage-related PD-L1 expression in Kaposi sarcoma tumor microenvironment. *Journal of Cutaneous Pathology*, 47(10):888-895.

DOI: <https://doi.org/10.1111/cup.13716>

Stage-related PD-L1 expression in Kaposi sarcoma tumor microenvironment

Beatrice Joest MD¹  | Werner Kempf MD^{2,4} | Arbeneshe Berisha BSc² | Peter Peyk PhD³ | Michael Tronnier MD¹ | Christina Mitteldorf MD⁵

¹Department of Dermatology, HELIOS-Klinikum Hildesheim, Hildesheim, Germany

²Kempf und Pfaltz, Histologische Diagnostik, Zürich, Switzerland

³Department of Consultation-Liaison-Psychiatry and Psychosomatic Medicine, University Hospital Zürich, Zürich, Switzerland

⁴Department of Dermatology, University Hospital Zürich, Zürich, Switzerland

⁵Department of Dermatology, Venereology and Allergology, University Medical Center Göttingen, Göttingen, Germany

Correspondence

Christina Mitteldorf, MD, Clinic of Dermatology, Venereology and Allergology, University Medical Center Göttingen, Robert-Koch-Strasse 40, 37075 Göttingen, Germany. Email: christina.mitteldorf@med.uni-goettingen.de

Abstract

Background: The immune checkpoint molecule PD-L1 represents an important target in oncological immune therapy. The aim of our study was to evaluate PD-L1 expression and the composition of the tumor microenvironment (TME) in Kaposi sarcoma.

Methods: Immunohistochemical stains were performed for PD-L1, CD3, CD33, CD68, and CD168 in 24 Kaposi sarcoma samples. In PD-L1-positive cases, the double stains for PD-L1, CD31, podoplanin, and HHV8 were added.

Results: PD-L1 was observed in 71% of the samples and was predominantly located in the TME. PD-L1 expression was significantly higher in nodular stage than in patch/plaque stage. The TME consisted of CD68+/CD163+ macrophages, CD33+ myeloid-derived suppressor cells and monocytes and CD3+ T-cells. The TME showed a peritumoral distribution in nodular stage, in contrast to a diffuse distribution in patch/plaque stage. In 12 samples (50%), no plasma cells were found.

Conclusion: In nodular stage of KS, the TME is pushed back in the periphery of the tumor nodules. The PD-L1-positive TME between the tumor cells might protect them from the immune attack. An anti-PD-L1 treatment might be promising in KS patients.

KEYWORDS

Kaposi sarcoma, macrophages, PD-L1, plasma cells, tumor microenvironment

1 | INTRODUCTION

Kaposi sarcoma (KS) is a HHV-8 (human herpes virus type 8)-associated vascular proliferation.¹⁻³ As mentioned in most dermatopathological textbooks⁴⁻⁶ and by the current World Health Organization (WHO) classification for skin tumors,³ the tumor seems to be accompanied by plasma cells, which has been considered as an important diagnostic indicator. Furthermore, T cells, activated B cells, dendritic cells, monocytes, and tumor-associated macrophages

(TAMs) have been identified as components of the tumor microenvironment (TME) in Kaposi sarcoma.^{1,7,8}

The interaction between the immune system and the tumor cells is essential for cancer defense and cancer survival. This interaction is determined by several complex pathways.⁹ One of these pathways is the signaling between PD-1 (programmed cell death 1) and its ligands PD-L1 and PD-L2.⁹ PD-L1 is an immunomodulatory cell-surface glycoprotein, belonging to the B7 family.^{10,11} Its expression is reported in many tumor cells, tumor infiltrating lymphocytes, and TAMs in various solid tumors. PD-L1 expression has been extensively studied in various skin malignancies.¹²⁻¹⁶ Beyond melanoma, PD-L1 expression

Beatrice Joest was involved in a part of doctoral thesis.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. Journal of Cutaneous Pathology published by John Wiley & Sons Ltd.